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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
10/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/593,256	TAVITIAN ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *7-36 and 38-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,37 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2006* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-6, 37 and 45, in the reply filed on 7/26/10 is acknowledged. The traversal is on the ground(s) that the Examiner has not provided any indication that the contents of the claims interpreted in light of the description was considered in making the assertion of a lack of unity and therefore has not met the burden necessary to support the assertion. Furthermore, 37 C.F.R. § 1.475(b) states in pertinent part: "An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (2) A product and a process of use of said product;..." In addition, The MPEP §806.03 states: "Where the claims of an application define the same essential characteristics of a single disclosed embodiment of an invention, restriction there between should never be required. This is because the claims are not directed to distinct inventions; rather they are different definitions of the same disclosed subject matter, varying in breadth or scope of definition." This is not found persuasive because

each group of invention has a different technical feature. For examples, the technical feature for the Group I invention is a method of identifying for ligands specific for RPTK using various components; the technical feature of Group II is an aptamer compound. Therefore, Groups 1-VII are not so linked by the same or a corresponding special technical feature as to form a single inventive concept. In addition, the special technical feature of Group II is known in the prior art. For example, Chen discloses an aptamer. Therefore, the inventions lack unity, as demonstrated by showing the common technical features does not "define a contribution over the prior art". See MPEP 1850.

The requirement is still deemed proper and is therefore made FINAL.

Applicants provisional election, for examination purposes only, the following species: 1) aptamers (at least claim 1 readable thereon); 2) biological activity: reversion of the phenotype associated with activation of the RPTK (at least claim 6 readable thereon); 3) receptor protein-tyrosine kinase: RET receptor (at least claim 8 readable thereon) is also noted.

Status of Claims

Claims 1-45 are pending.

Claims 7-36 and 38-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species.

Claims 1-6, 37 and 45 are under examination.

Specification

The disclosure is objected to because of the following informalities:

1. It contains an embedded hyperlink and/or other form of browser-executable code. See e.g., page 27, line 36 and page 28, line 2.

2, There are no sequence identifier number for the sequences at e.g., page 41.

Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's

cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 37 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants are in possession of a method describing Pc12 cells expressing a Ret receptor mutated in the intracellular and extracellular domains and contacting with modified aptamer library of 2-F-py-RNAs. Applicants are not in possession of a method of identifying e.g., aptamers for RPTK wherein the intracellular and extracellular domain of any cell has been

mutated in every conceivable way. The method claims not only enormous cells but also a huge type of mutations intracellularly or extracellularly in the cells. Claim 45 lists Seq. ID. 1 and 2 or a fragment of at least 8 nucleotides of these sequences as the starting nucleic acid combinatorial library but does not define the randomization therein. An adequate written description of a chemical invention requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described."). See MPEP 2163. One skilled in the art would have been able to make

and use the full scope of the claim method drawn to a mutated Ret receptor in PCl cells through routine experimentation. However Applicants did not describe the invention of claim 1 sufficiently to show they had possession of the claimed genus method using e.g., any aptamers for any RPTK in cells mutated intra and extracellularly. See, e.g., Noelle V. Lederman, 355 F.3D 1343, 96 USPQ2dI508, 1513 (Fed. Cir 2004) ("invention is, for purposes of the 'written description' inquire, whatever is now clamed"). Applicants have disclosed only 2-F-Py-RNA aptamer as the mixture of nucleic acids and cells expressing Ret mutated at a single location, e.g., intracellularly (RetM198T). Therefore, the skilled artisan cannot envision all the contemplated aptamers, cells and RPTK possibilities recited in the instant claim method. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiefs v. Revel, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.II2, ¶1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through

sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column). Vas-Cath Inc. v. Mahurkar, 19 USPQ2d iiii, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116. Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. Applicants are directed to the final Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, [1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 37 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The terms "specific", "high affinity" and "enriched" in claim 1; "suitable" in claim 2 and "fixed" in claim 37 are relative terms which render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

2. Claim 1, step (c) recites the limitation "the same cell type as the CTe cells" and "the cell-nucleic acid complexes",

claim 1, step f; "the starting nucleic acid combinatorial library" in claim 3, 37 and 45. There is insufficient antecedent basis for this limitation in the claim.

3. Claim 1, step f is vague and indefinite at to the term "i.e.".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 37 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (PNAS, 8/2003) in view of Yayon et al (USP 7498416).

Chen et al discloses at e.g., page 9226, col. 2; a method of identifying RNA aptamers against RTKs. Libraries of randomized RNAs is screened in vitro using SELEX. RNA aptamers used can be with fluorine in the 2' position which significantly enhances the half-life of RNA aptamers in serum. Aptamers have

been selected successfully against several extracellular protein ligands, such as vascular endothelial growth factor (VEGF). As a target for aptamer selection, RTKs stand out through their large size. Chen has successfully selected RNA aptamers against the ECD of HER3 and evaluated one aptamer in particular to demonstrate its potential for the analysis of RTK interactions and its potential use as an inhibitor against cancer cells.

Chen discloses at page 9227, col. 1 up to page 9230, col. 2 the method as comprising producing single-stranded DNA templates for SELEX that includes contiguous randomized positions flanked by constant regions (Fig. 1). The constant regions included targets for PCR primers and cloning sites and a promoter. A filter binding assay was used for the first eight rounds of selection. The RNA pool was first counterselected by passing through a filter. The counterselected RNAs were then incubated with HER3ECD. Over the course of selection the ratio of protein to RNA was gradually lowered from 4:1 to 1:2. Unbound aptamers were separated from protein-bound aptamers. A gel-shift assay was used in the last seven rounds of selection. RNA was incubated with HER3ECD as described above. Gel electrophoresis was carried out. The retarded band was isolated, and RNA was extracted from the gel in elution buffer. For both selection methods, the RNA was subsequently reverse-transcribed into cDNA

Finally, the cDNA was PCR-amplified for the next round of selection. The bound and unbound aptamer was measured and identified. Chen does not teach that the tyrosine kinase receptor, HER3 is mutated at the extracellular and intracellular region. However, Yayon discloses at e.g., col.24, line 35+; that other screens can be carried out on cell lines expressing a RPTK carrying a mutation, such as the FDCP-FR3 each line expressing the FGFR3 achondroplasia mutation. The receptors of this line become constitutively active, e.g. are able to signal in the absence of a ligand as determined by ERK (MAPK) phosphorylation, a downstream effector. Ret receptor is disclosed by Yayon at e.g., col. 19, line 60. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to mutate the tyrosine kinase receptor of Chen in the manner taught by Yayon. One would have a reasonable expectation of success since its counterpart, the unmutated part has been successfully screened by Chen using SELEX method. One would be motivated to mutate the receptor as it becomes constitutively active, e.g. are able to signal in the absence of a ligand as determined by ERK (MAPK) phosphorylation, a downstream effector as taught by Yayon.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639